REMARKS

Claims 27-34 are pending in this application.

Applicants respectfully traverse the present rejections and request continued examination in light of the newly submitted evidence and arguments.

Rejection under 35 U.S.C. § 101:

Claims 27-34 stand rejected under 35 U.S.C. §101 as allegedly not supported by either an asserted utility that is specific and substantial or by a well-established utility. Applicants respectfully disagree with the maintained rejection of claims 27-34 for the following reasons.

The courts have made clear that the threshold of utility is not high. An invention is "useful" under § 101 if it is capable of providing some identifiable benefit. *Juicy Whip Inc. v. Orange Bang Inc.,* 185 F.3d 1364, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999). The PTO also acknowledges that the threshold is not high and cautions that rejections for lack of utility are rarely sustained by federal courts. MPEP § 2107.02 III B, citing *In re Gazave,* 379 F.2d 973 (CCPA 1967) (emphasis in original). Indeed, the caselaw demonstrates that a utility rejection is not proper unless the PTO establishes that it has reason to doubt the objective truth of the statements contained in the written description. The PTO may establish a reason to doubt an inventor's asserted utility when:

(1) the written description suggests an inherently unbelievable undertaking; or

(2) the written description suggests a utility that involves implausible scientific principles.

In re Cortright, 165 F.3d 1353, 49 USPQ2d 1464 (Fed. Cir. 1999).

When the proper standards are applied, the PTO cannot establish a reason to doubt Applicants' asserted utility in this case because Applicants' asserted utility does not involve either an inherently unbelievable undertaking or implausible scientific principles.

Indeed, Applicants' asserted utility should be accepted because it is squarely within the teaching of leading textbooks in the field, and is supported by numerous references and the declarations of skilled experts.

In addition, the PTO has accepted a substantially identical assertion of utility in at least 16 other patents and applications with evidence supporting the assertion of utility that is substantially similar to the evidence relied on in the present case. Applicants previously identified U.S. Patent No. 7,208,308, which shares a similar specification and assertion of utility with the present invention, as evidence that the PTO views Applicants' asserted utility as sufficient to satisfy the utility requirement. The Office action rejects Applicants' reliance on the '308 patent because, according to the Office action, the Examiner is precluded from commenting on the issuance of the '308 patent. Applicants however are not requesting that the Examiner comment upon issuance or allowance of that patent. Instead, Applicants cite that patent as one example of the PTO's view that Applicants' asserted utility is sufficient. The Court of Customs and Patent Appeals recognized that "similar claims allowed by the Patent Office tribunals furnish evidence of what features those tribunals regard as patentable." *In re Schecter and LaForge,* 205 F.2d 185, 98 USPQ 144, 150 (CCPA 1953). Thus, allowed claims based on a substantially similar application, supported by a substantially identical assertion of utility based on substantially similar data is persuasive evidence that should be considered in examining the presently claimed invention.

Moreover, the PTO has acknowledged that a utility such as that asserted in the present application is sufficient by allowing or issuing at least the following patents and applications: U.S. Patent Nos. 7,208,308, 7,279,551, 7,282,566, 7,282,559, 7,282,560, 7,282,569; US Patent App. Ser. Nos. 10/123,214 (Notice of allowance mailed 6/14/07); 10/140,863 (Notice of allowance mailed 6/21/07); 10/141,755 (Notice of allowance mailed 6/20/07); 10/142,762 (Notice of allowance mailed 6/14/07); 10/143,113 (Notice of allowance mailed 6/12/07); 10/230,417 (Notice of allowance mailed 5/30/07); 10/181,000 (Notice of allowance mailed 6/7/07); 10/187,886 (Notice of allowance mailed 6/21/07); 10/187,739 (Notice of allowance mailed 6/21/07); and 10/219,077 (Notice of allowance mailed 6/18/07). Each of these issued patents and allowed applications include a

substantially identical assertion of utility as the utility asserted in the present application. In addition, all of the specifications are substantially similar to the present specification, as is the supporting data. Thus, allowance and issuance of these 16 patents and applications, which were examined by at least 10 different examiners, is persuasive and direct evidence that Applicants' assertion of utility satisfies the requirements of 35 U.S.C. § 101.

Moreover, as stated above, the courts have recognized that a PTO rejection based on lack of utility is only proper when the asserted utility is unbelievable or involves implausible scientific principles. If the PTO can establish either of these premises, then the PTO may properly challenge an applicant's asserted utility. Once a claim is properly challenged for lack of utility, an applicant may overcome that rejection by showing that it is more likely than not that the claims are supported by the asserted utility. Significantly, no explicit evidence of the asserted utility is required.

For example, in a related field, the pharmaceutical arts, practical utility may be shown by adequate evidence of any pharmacological activity. Thus, although testing may be required to establish practical utility, that testing need not absolutely prove that the compound is pharmacologically active. Rather, all that is required is that the tests be reasonably indicative of the desired pharmacological response. In other words, there must be a sufficient correlation between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a ***reasonable*** probability, that the novel compound will exhibit the asserted pharmacological behavior. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 39 USPQ2d 1895 (Fed. Cir. 1996). A rigorous correlation, which appears to be required by the present Office action is not required; a reasonable correlation is sufficient. *Id.*

Here, Applicants have disclosed sufficient test results to demonstrate to a ***reasonable*** probability that the claimed polypeptide will exhibit the asserted activity, overexpression in lung or colon tumors. Specifically, the present application describes a gene amplification analysis that was conducted in connection with PRO357 nucleic acid

sequences and the specification sets forth the amplification values, measured as ΔCt, for PRO357. A ΔCt value of at least 1.0 — Dr. Goddard testified that one of ordinary skill views ΔCt values great than 1 as significant and indicating the amplified gene is useful as a diagnostic marker — was observed for PRO357 in 26 of the tested tumors and tumor cell lines listed in Table 9. *See* paragraph 7 of the Goddard Declaration. Indeed, PRO357 showed gene amplification of approximately 1.05 to 3.51 ΔCt units, which corresponds to $2^{1.05}$ to $2^{3.51}$ fold amplification in primary lung and colon tumors and tumor cell lines. These ΔCt data values demonstrate that PRO357 is significantly amplified in approximately 93% of lung tumor tissues and approximately 75% of colon tumor tissues listed in Table 9.

Moreover, the data in the present application is also supported by the declarations of Paul Polakis and Randy Scott and by the references previously submitted by Applicants in support of their assertion of utility. The Office action alleges that the Polakis and Scott Declarations are not persuasive because those declarations do not contain any information specific to PRO357 mRNA expression or PRO357 polypeptide expression. However, Applicants respectfully submit that the Polakis and Scott Declarations are persuasive evidence supporting Applicants' assertion of utility when viewed in the proper context. The nature of the fact sought to be established in these declarations is that under the proper utility standard, the gene amplification observed for PRO357 more likely than not correlates to overexpression of the PRO357 polypeptide. This fact is adequately established and supported. Dr. Polakis (Polakis II) declared "in the cases where we have been able to quantitatively measure both (i) mRNA and (ii) protein levels in both (i) tumor tissue and (ii) normal tissue, we have observed that in the vast majority of cases, there is a very strong correlation between increases in mRNA expression and increases in the level of protein encoded by that mRNA." Similarly, Dr. Scott unequivocally confirms that, as a general rule, there is a good correlation between mRNA and protein levels in a particular tissue. This conclusion, which states a general rule observed over time, is based on the stated facts that Dr. Scott has more than 15 years experience with microarray technologies, and in his experience, Dr. Scott has noticed a good correlation. Accordingly, the Polakis and Scott Declarations support

Applicants' assertion of utility and provide significant evidence that Applicants' assertion of utility satisfies the utility standard.

In addition, although there may be some opposing evidence, Applicants have cited substantial evidence supporting their assertion of utility. Opposing evidence does not necessarily demonstrate that an applicant's assertion of utility is insufficient to satisfy the utility requirement. Indeed, the applicant needs only to show that the asserted utility is *more likely than not.* This standard acknowledges that there may be some evidence that opposes Applicants' assertion of utility yet the utility requirement still may be satisfied. In the present case, the majority of the art references cited and discussed during prosecution demonstrate that gene amplification is art recognized to correlate with mRNA levels and polypeptide expression levels. Such evidence is enough to support Applicants' assertion of utility in this case because the law does not require that the asserted utility be based on a correlation that "always" occurs; it only must be more likely to occur than not.

Thus, as recognized by the PTO in allowing 16 U.S. patent based on a similar utility, gene amplification is an essential mechanism for oncogene activation and in general gene amplification more likely than not correlates with protein overexpression. In the present case then, it is more likely than not that the gene amplification demonstrated for PRO357 correlates with protein overexpression of PRO357. This is sufficient to satisfy the utility requirement, particularly because consideration of the totality of the evidence clearly demonstrates that Applicants' asserted utility is specific, substantial, and credible. Applicants have overcome this ground of rejection and respectfully request it be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph:
Enablement

The Examiner contends that because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention. Applicants respectfully disagree. As

discussed above, the claimed invention is adequately supported by an asserted utility that is both specific and substantial. Applicants respectfully request the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112 ¶1 for alleged inadequate disclosure on how to use the claimed invention.

Claim Rejections under 35 U.S.C. § 102(b)

The Office action rejects claims 27-34 under 35 U.S.C. § 102(b) as being anticipated by Botstein *et al.* (WO 99/35170, published 7/15/99). Anticipation under 35 U.S.C. § 102(b) requires that "the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, *more than one year prior to the date of application for patent in the United States.*"

An application for a patent based on the present invention was filed at least as early as December 22, 1998, which is prior to the publication date of the cited reference. In particular, the PRO357 polypeptide and amino acid sequences are disclosed in U.S. Provisional Application Serial No. 60/113,296 ("the '296 application"), filed 12/22/1998. More specifically, the nucleic acid sequence encoding PRO357 is identified as DNA44804 and is shown in Figure 15 (SEQ ID NO:15) of the '296 application. This sequence corresponds to Figure 25 (SEQ ID NO:68) in the present application. The amino acid sequence encoding PRO357 is shown in Figure 16 (SEQ ID NO:16) of the '296 application, which corresponds to Figure 26 (SEQ ID NO:69) in the present application. In addition, the gene amplification experiment described in Example 28 of the present specification is described in Example 2 of the '296 application. For the reasons discussed above, description of the gene amplification assay in the '296 application satisfies the utility and enablement requirements.

As an application for a patent based on the present invention was filed at least as early as December 22, 1998, Applicants respectfully submit that rejection of claims 27-34 under 35 U.S.C. § 102(b) based on the Botstein reference (WO 99/3517, published 7/15/99) is improper and respectfully request that this ground of rejection be withdrawn.

CONCLUSION

Applicants respectfully request the Examiner grant allowance of claims 27-34. The Examiner is invited to contact the undersigned attorney for the Applicant via telephone if such communication would expedite this application.

Respectfully submitted,

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